REMARKS

Applicant has made amendments to the title, specification, and abstract to correspond to the claims. No new matter is added to the application.

Claims 23, 25, 26 and 28-40 are canceled and replaced with claims 45-71.

Applicant believes claims 45-71 comply with 35 U.S.C. § 112. For instance, independent claim 45 makes clear that the device is the subject matter being claimed. Dependent claims 46-48 an 50-51 make clear that the combination of the device and an instrument is the subject matter of those claims. Also, the phrase "enclosed by the body" found vague and indefinite by the Examiner is not in claims 45-71.

Claims 23, 28, 3-33, and 35-37 were rejected under 35 U.S.C. § 102(b) as anticipated by Handique (P/N 6,130,098). Claims 23, 25, 28, 30-38 and 40 were rejected under 35 U.S.C. § 103(a) as being obvious over Handique (6,130,098) in view of Wilding (P/N 5,587,128).

Applicant request reconsideration of these rejections, as now applicable to claims 45-71, in view of the following arguments.

Independent Claims 45 and 60

Applicants submit that independent claim 45 is patentable over Handique alone or in combination with Wilding because no combination of these references teaches an apparatus having:

a transition region connecting a reaction chamber to a separation channel, wherein the portion of the body defining the transition region has sufficiently low thermal conduction so that the transition region substantially thermally isolates the reaction chamber from the separation channel; and

at least one valve in the transition region for controlling fluid flow between the reaction chamber and the separation channel.

Handique fails to teach or suggest these elements of the applicants' claim. Although Handique does suggest one embodiment of his microscale devices may have a valve (Fig. 13, in which a valve is present in a side channel connecting to a main channel), Handique fails to teach or suggest a critical element in applicants' claim 45, specifically a valve in a transition region connecting a reaction chamber to a separation channel.

In Fig. 1, Handique shows a device having a reaction chamber connected to an electrophoresis module, but no valve is shown in the region connecting the reaction chamber to the electrophoresis module. In describing Fig. 1, Handique teaches that "sample and reagent are injected into the device through entry ports (A) and they are transported as discrete droplets through channels (B) to a reaction chamber, such as a thermally controlled reactor where mixing and reactions (e.g., restriction enzyme digestion or nucleic acid amplification) occur (C). The biochemical products are then moved by the same method to an electrophoresis module (D) where migration data is collected by a detector (E) and transmitted to a recording instrument (not shown)." (column 13, lines 22-31). Thus, there is no teaching of a valve in the transition region connecting the reaction chamber to the electrophoresis module.

In fact, in the next section of the specification, when describing how these discreet droplets are created and moved through the system, Handique teaches that "The present invention contemplates methods, compositions and devices for the creation of microdroplets of discrete (i.e. controlled and predetermined) size. The present invention contemplates the use of selective hydrophobic coatings to develop a liquid-sample injection and motion system that does not require the use of valves." (Column 13, lines 61-66).

Thus, Handique teaches very different structure than that recited in claim 45. The Wilding reference also fails to teach or suggest a device having a valve in a transition region that connects a reaction chamber to a separation channel. Thus, neither Handique alone nor the combination of Handique and Wilding anticipates nor makes obvious the applicants' invention as recited in claim 45 or claim 60.

Handique also fails to teach or suggest that the portion of the body defining the transition region has sufficiently low thermal conduction so that the transition region substantially thermally isolates the reaction chamber from the separation channel. In Fig. 1 of Handique, the reaction chamber and electrophoresis area are etched in the same, rectangular, conductive substrate and there is no teaching or suggestion that the transition region connecting the reaction chamber to the electrophoresis area thermally isolate the reaction chamber from the electrophoresis area. The Wilding reference also fails to teach or suggest this feature . Thus, neither Handique nor the combination of Handique and Wilding anticipates the applicants' invention as recited in claim 45 or claim 60.

Applicant's device and method, as recited in claims 45 and 60, provides important advantages, such as the ability to heat a sample in a reaction chamber of a device and to separate components of the sample in a separation channel in the same device without the heat from the reaction chamber degrading performance in the separation channel. In addition, applicant's device and method provide superior control of fluid between the reaction chamber and separation channel. High internal pressure can develop in a reaction chamber due to the thermal expansion of liquid or gas present in the chamber, the generation of gas bubbles, or the chemical reactions performed inside of the chamber. This pressure, combined with any elevated temperatures within the chamber, can cause the unwanted flow or diffusion of chemicals from the reaction chamber into the separation channel. Applicants' device and method overcomes this problem.

For at least the foregoing reasons, independent claims 45 and 60 and claims 46-59 and 61-71 depending therefrom are patentable.

CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-752-2469.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE TITLE:

Please replace the title with the following title:

--INTEGRATED SAMPLE ANALYSIS DEVICE--

IN THE SPECIFICATION

Please replace the paragraph beginning on page 4, line 15 with the following paragraph:

--The present invention provides an integrated reaction and separation device that overcomes the disadvantages of the prior art discussed above. [In particular, the integrated device of the present invention avoids the use of inconvenient bonding techniques, enabling inexpensive, high-volume production of the device. Additionally, the integrated device includes a reaction chamber that is thermally isolated from the separation region, thereby enabling proper heating of a sample without degrading the separation region.]--

Please replace the paragraph beginning at page 4, line 22, with the following paragraph (twice amended):

--In a preferred embodiment, the device comprises a body, preferably a molded polymeric part, having formed therein a reaction chamber for chemically reacting a sample, a separation region for separating components of the sample, and a transition region connecting the reaction chamber to the separation region. [The reaction chamber, transition region, and separation region are formed in and enclosed by the body.] Additionally, the device includes at least one valve in the transition region [includes at least one flow restrictor] for controlling the flow of fluid between the reaction chamber and the separation region. Further, the portion of the body defining the transition region has [lower] sufficiently low thermal conduction [than the portion of the body defining the

reaction chamber] so that the transition region substantially thermally isolates the reaction chamber from the separation region.--

Please replace the paragraph beginning on page 5, line 4 with the following paragraph (twice amended):

--The body may be surrounded by external, functional components such as differential pressure sources, electro-motive sources, heaters, light sources, and optical detectors. In the preferred embodiment, the reaction chamber is an amplification chamber for amplifying nucleic acid in the sample. Also in the preferred embodiment, the separation region comprises a separation channel, e.g., an electrophoresis column or capillary containing a suitable matrix material, such as electrophoresis gel or buffer, for separating nucleic acid fragments in the sample. In one embodiment, the device further includes at least two electrodes coupled to the body, the electrodes being positioned to induce the sample components to separate into bands in the separation channel when a voltage difference is applied between the electrodes.--

IN THE ABSTRACT

Please replace the abstract on page 28 with the following abstract of the disclosure:

--A device for analyzing a sample comprises a body having, a reaction chamber for conducting a reaction, a separation channel for separating components of the sample, and a transition region connecting the reaction chamber to the separation channel. The portion of the body defining the transition region has sufficiently low thermal conduction so that the transition region substantially thermally isolates the reaction chamber from the separation channel. The device also includes at least one valve in the transition region for controlling fluid flow between the reaction chamber and the separation channel. At least two electrodes are coupled to the body, the electrodes being positioned to induce the sample components to separate into bands in the separation channel when a voltage difference is applied between the electrodes.

[A sample-processing device [150] comprises a unitary body [152], preferably a molded polymeric part, having formed therein a reaction chamber [154] for chemically reacting a sample, a separation region [158] for separating components of the sample, and a transition region [156] connecting the reaction chamber [154] to the separation region [158]. The reaction chamber [154], transition region [156], and separation region [158] are formed in and enclosed by the unitary body [152]. Additionally, the transition region [156] includes at least one flow restrictor [180] for controlling the flow of fluid between the reaction chamber [154] and the separation region [158]. Further, the portion of the unitary body [152] defining the transition region [156] has lower thermal conduction than the portion of the body defining the reaction chamber [154] so that the transition region [156] thermally isolates the reaction chamber [154] from the separation region [156]. In a preferred embodiment, the reaction chamber [154] is an amplification chamber for amplifying nucleic acid in the sample, and the separation region [158] comprises an electrophoresis column or capillary containing a suitable matrix material, such as electrophoresis gel or buffer, for separating nucleic acid fragments in the sample. Electrodes [167, 168, 169] are embedded in the body [152] for forcing the sample to flow from the reaction chamber [154] to the separation region [158]. The unitary body [152] may also be surrounded by external, functional components such as an optical detector [186] for detecting separated components of the sample.]--